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Addendum: Reconstructing sentence processing in aphasia

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1. Introduction:

This document outlines the protocol changes made due to the COVID-19 pandemic. Recruitment and testing for the trial were paused in March 2020, and the trial will resume once Public Health guidance and research site regulations (UCL) permit recruitment and testing of participants with neurodisability. The new overall trial end date is 31/05/2023.

2. Protocol changes:

Due to the impact of the COVID-19 pandemic on the trial timeline and subsequent participant recruitment, the original protocol was modified in order to reduce the number of study conditions, allowing an adequately powered study. The modifications also allowed adherence to social distancing guidelines, and led to a shorter protocol and adequate ventilation of research spaces between participants. The following changes were made:

a) deletion of non-invasive brain stimulation (transcranial direct current stimulation, tDCS) adjunct therapy,

b) addition of a baseline MR scan to allow pre-/post-therapy comparison of changes in resting state connectivity for those participants eligible for MRI scanning.

The following sub-sections outline the changes in more detail.

a. Research Questions:

(1) Does the computerised behavioural therapy improve connected speech production and spoken sentence comprehension in comparison to waitlist/usual care control;

(2) What is the relationship between treatment outcome and demographic, behavioural variables, lesion size and location;

(3) What is the relationship between treatment outcomes and changes in measures of resting state functional connectivity within and between the left-hemisphere language network and its right-hemisphere homologue;

(4) What is the impact of the intervention on perceptions of quality-of-life, and on an untreated control language behaviour.

b. Methods:

i. Participants:

Our original aim was to recruit 66 participants in the trial, but in light of the pandemic and reduced recruitment time, the target is reduced to 30 adults with post-stroke aphasia and impairments in spoken sentence comprehension and/or production.

ii. Inclusion and exclusion criteria:

The removal of tDCS from the trial design allows for recruitment of a broader spectrum of participants to the behavioural study. Updated exclusion criteria for the study are:

- Significant other neurological disorder (e.g., neurodegenerative illness)
- History of speech and language disorder prior to stroke (e.g., developmental dyslexia)
- Current involvement in another therapy trial

iii. Conditions:

Our original study design examined the combined effects of behavioural therapy and tDCS on sentence processing impairment in post-stroke aphasia. With the elimination of the active/sham tDCS conditions, participants are now randomised to one of two conditions after the first baseline evaluation:

- behavioural therapy with immediate trial entry
- behavioural therapy with deferred trial entry

Randomisation: 1:1 immediate vs deferred (not stratified by sex), using block randomisation and random generation of 0/1 codes within each block. Researchers are blind to block size.

iv. MRI scans:

Two MR brain scans (pre-therapy and post-therapy) will be performed instead of a single scan as in the original protocol. This will enable us to enhance the neuroscience component of the study. Participants who are not eligible for MR scanning (as determined by standard MR safety screening) are still able to receive the behavioural therapy.

Prior to the intervention, participants are screened for MR safety and, if safe, will have a structural MRI brain scan (1.5T Siemens Avanto scanner) to determine the integrity of tissue in the left inferior frontal region, and the location and extent of lesion. We will record numbers of volunteers who are excluded from this element of the trial on the basis of safety criteria and monitor the impact on overall imaging data available for analysis. Resting state functional MRI scans pre- and post-intervention will also be employed to explore changes in resting state connectivity associated with behavioural intervention. Measures of functional connectivity quantify the extent to which activity in separate cortical regions is correlated, and cortical regions with positively-correlated activity are presumed to facilitating a common functional goal. Changes in measures of functional connectivity within the left hemisphere language network or its right hemisphere homologue, or interhemispheric changes in language cortex functional connectivity will provide evidence that behavioural intervention is associated with neural reorganisation of language networks.

v. Intervention

The dose level employed in this study changed from 3-hours per week for 4-weeks in the original protocol to 2-3-hours per week for 4-weeks in the updated protocol. Each participant will complete a total of 12 therapy sessions over the 4-week therapy phase (3 sessions per week). Each session lasts for approximately 45-60 minutes (including breaks).

vi. Recruitment materials:

Updated subject information sheet and online recruitment materials can be found here:

http://www.cognitionandgrammar.net/s/Sentence_Therapy_Information_Sheet.pdf

https://www.youtube.com/watch?v=bu_ZfvNdPZY